UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,259	12/21/2005	Jackie Papkoff	DEX0491US.NP	9408

32800 7590 10/10/2007

LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
NATARAJAN, MEERA	
ART UNIT	**PAPER NUMBER**
1643	

NOTIFICATION DATE	DELIVERY MODE
10/10/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/562,259	PAPKOFF ET AL.	
	Examiner	Art Unit	
	Meera Natarajan	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6,8,10,16,19,20,22,23,30,31,35,37,39,47 and 61-63* is/are pending in the application.

4a) Of the above claim(s) *30,31,35,37,39,47 and 61-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,8,10,16,19, 20, 22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/10/2006 and 02/21/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I and species election "cytotoxic agents", "toxins", and "ovarian cancer" in the reply filed on 08/19/2007 is acknowledged. The traversal is on the ground(s) that the reference Antalis et al. recited in the restriction requirement does not teach all the elements of Claim 1. This is not found persuasive because as stated in the restriction requirement Antalis et al. teach antibodies directed to testisin, also known as Pro104. Antalis et al. also discloses methods of use for the antibodies involving in vivo therapeutic uses for testicular cancer and fertility/infertility disorders (see column 15, last paragraph and column 18 paragraph 4). The requirement is still deemed proper and is therefore made FINAL.

2. Claims 30, 31, 35, 37, 39, 47, and 61-63 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 08/19/2007.

3. Claims 1-3, 6, 8, 10, 16, 19, 20, 22 and 23 will be examined on the merits.

Specification

4. The disclosure is objected to because of the following informalities: several trademarks are denoted on p.24 of the specification. Appropriate correction is required.

5. The use of the trademarks has been noted in this application on p.24. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 6, 19 and 23 drawn to antibodies produced by the following hybridomas; Pro104.C25.1, Pro104.D9.1 and Pro104.K81.15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

7. The claims 6, 19 and 23 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

8. It is unclear if a cell line which produces an antibody having the exact chemical identity of the Pro104 antibody produced by hybridomas Pro104.C25.1, Pro104.D9.1 and Pro104.K81.15 is known and publicly available, or can be reproducibly isolated

without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

9. For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species. The specification discloses on p.148-149 three hybridomas (PTA-6076, 6077 and 6078) deposited after the effective filing date of the instant application. Deposit of these three hybridomas along with all the required assurances would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

10. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological

materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

11. The specification lacks complete deposit information for the deposit of hybridomas Pro104.C25.1, Pro104.D9.1 and Pro104.K81.15. It is not clear that the antibody produced by the above hybridomas possessing the identical properties of the claimed Pro104 antibody are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

12. Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a monoclonal antibody and hybridoma identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

13. Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed antibody, a suitable deposit of hybridomas Pro104.C25.1, Pro104.D9.1 and Pro104.K81.15 for patent purposes, evidence of public availability of the claimed antibody or evidence of the reproducibility without undue experimentation of the claimed antibody, is required.

14. Applicant's referral to the deposit of hybridomas Pro104.C25.1, Pro104.D9.1 and Pro104.K81.15 as recited on pages 148-149 of the specification is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met. The deposit of hybridomas Pro104.C25.1, Pro104.D9.1 and Pro104.K81.15 were made after the effective filing date of the instant application.

15. If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit of hybridomas Pro104.C25.1, Pro104.D9.1 and Pro104.K81.15 has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

16. If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1, 3, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Antalis et al. (US Patent 6479274).

19. The Claims are drawn to a monoclonal antibody which binds Pro104 (also known as testisin as disclosed throughout the specification) on a mammalian cancer cell in vivo.

20. Antalis et al. teach antibodies that bind to testisin, also known as Pro104, and methods of use for the antibodies involving in vivo therapeutic uses for testicular cancer and fertility/infertility disorders (see column 15, last paragraph and column 18 paragraph 4). Therefore the reference teaches the limitations of Claims 1, 3, and 16.

21. Claims 1, 3, 16 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Bandman et al. (US Patent 6203979).

22. The Claims are drawn to a chimeric monoclonal antibody which binds Pro104 (also known as testisin as disclosed throughout the specification) on an ovarian cancer cell in vivo.

23. Bandman et al. teach the sequence SEQ ID NO:3 wherein amino acids 1-314 are identical to amino acids 1-314 of Pro-104 sequence disclosed in the instant application

recited as SEQ ID NO: 3 (total of 340 amino acids) (see attached sequences). The antibodies taught by Bandman et al. would comprise antibodies having epitopes that would bind to amino acids 1-314 of SEQ ID NO:3 of the instant application. Bandman et al. also teaches method of producing antibodies, including monoclonal, polyclonal or chimeric (see column 28), and in vivo use of said antibodies in the diagnosis, treatment, and prevention of cell proliferative disorders and cancers including ovarian (see column 26 line 59 through column 27 line 7). The antibodies taught by Bandman et al. are directed to inhibit and/or regulate the activity of human protease molecules. Bandman et al. disclose human protease molecules play a role in such activities as cell growth, differentiation, and apoptosis. Bandman et al. disclose that increases in specific protease levels are correlated with increased malignant properties of tumor cells (see column 3 lines 47-51).

Claim Rejections - 35 USC § 103

24. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

25. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

26. Claims 1-3, 8, 10, 16, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bandman et al. (US Patent 6203979) in view of Queen et al. (US Patent 6180370).

27. The claims are drawn to an isolated Pro104 antibody that binds to Pro104 on a mammalian cell in vivo wherein said antibody is a monoclonal, chimeric or humanized antibody, and conjugated to a toxin and inhibits the growth of ovarian cancer cells and a cell that produces said antibody.

28. The teachings of Bandman et al. are presented in the 102(b) rejection set forth above. Bandman et al. does not teach humanized antibodies conjugated to toxins which become internalized upon binding. This deficiency is made up for in Queen et al.

29. Queen et al. (Patent # 6180370) teach a method for preparing humanized immunoglobulins for novel therapeutic agents. Queen et al. discloses pharmaceutical compositions comprising the humanized antibodies and effector molecules such as chemical agents, proteins, toxins or drugs conjugated to the antibody for diagnostic and therapeutic use, wherein the toxin conjugated to the antibody is absorbed (ie: internalized) by the cell promoting cell death (see columns 19 4th paragraph - column 20 2nd paragraph).

30. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to humanize the antibodies taught by Bandman et

al. and conjugate them to toxins. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Queen et al. because humanized antibodies conjugated to toxins help to specifically target and kill tumor cells in vivo and minimizes binding to normal non-specific cells.

Conclusion

31. Claims 1-3, 6, 8, 10, 16, 19, 20, 22 and 23 are rejected.

32. No Claim is allowed.

33. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meera Natarajan whose telephone number is 571-270-3058. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

current application: Papkoff et al. SEQ ID: 3

<210> 3
<211> 340
<212> PRT
<213> Homo sapiens

<400> 3

Met Gly Ala Arg Gly Ala Leu Leu Leu Ala Leu Leu Leu Ala Arg Ala
1 5 10 15

Gly Leu Arg Lys Pro Glu Ser Gln Glu Ala Ala Pro Leu Ser Gly Pro
20 25 30

Cys Gly Arg Arg Val Ile Thr Ser Arg Ile Val Gly Gly Glu Asp Ala
35 40 45

Glu Leu Gly Arg Trp Pro Trp Gln Gly Ser Leu Arg Leu Trp Asp Ser
50 55 60

His Val Cys Gly Val Ser Leu Leu Ser His Arg Trp Ala Leu Thr Ala
65 70 75 80

Ala His Cys Phe Glu Thr Tyr Ser Asp Leu Ser Asp Pro Ser Gly Trp
85 90 95

Met Val Gln Phe Gly Gln Leu Thr Ser Met Pro Ser Phe Trp Ser Leu
100 105 110

Gln Ala Tyr Tyr Thr Arg Tyr Phe Val Ser Asn Ile Tyr Leu Ser Pro
115 120 125

Arg Tyr Leu Gly Asn Ser Pro Tyr Asp Ile Ala Leu Val Lys Leu Ser
130 135 140

Ala Pro Val Thr Tyr Thr Lys His Ile Gln Pro Ile Cys Leu Gln Ala
145 150 155 160

Ser Thr Phe Glu Phe Glu Asn Arg Thr Asp Cys Trp Val Thr Gly Trp
165 170 175

Gly Tyr Ile Lys Glu Asp Glu Ala Leu Pro Ser Pro His Thr Leu Gln
180 185 190

Glu Val Gln Val Ala Ile Ile Asn Asn Ser Met Cys Asn His Leu Phe
195 200 205

Leu Lys Tyr Ser Phe Arg Lys Asp Ile Phe Gly Asp Met Val Cys Ala

210 215 220

Gly Asn Ala Gln Gly Gly Lys Asp Ala Cys Phe Gly Asp Ser Gly Gly
225 230 235 240

Pro Leu Ala Cys Asn Lys Asn Gly Leu Trp Tyr Gln Ile Gly Val Val
245 250 255

Ser Trp Gly Val Gly Cys Gly Arg Pro Asn Arg Pro Gly Val Tyr Thr
260 265 270

Asn Ile Ser His His Phe Glu Trp Ile Gln Lys Leu Met Ala Gln Ser
275 280 285

Gly Met Ser Gln Pro Asp Pro Ser Trp Pro Leu Leu Phe Phe Pro Leu
290 295 300

Leu Trp Ala Leu Pro Leu Leu Gly Pro Val Asp Pro Ala Phe Leu Tyr
305 310 315 320

Lys Val Val Arg Ser Arg Met Ala Ser Tyr Pro Tyr Asp Val Pro Asp
325 330 335

Tyr Ala Ser Leu
340

<210> 4
<211> 314
<212> PRT
<213> Homo sapiens

<400> 4

Met Gly Ala Arg Gly Ala Leu Leu Leu Ala Leu Leu Leu Ala Arg Ala
1 5 10 15

Gly Leu Arg Lys Pro Glu Ser Gln Glu Ala Ala Pro Leu Ser Gly Pro
20 25 30

Cys Gly Arg Arg Val Ile Thr Ser Arg Ile Val Gly Gly Glu Asp Ala
35 40 45

Glu Leu Gly Arg Trp Pro Trp Gln Gly Ser Leu Arg Leu Trp Asp Ser
50 55 60

His Val Cys Gly Val Ser Leu Leu Ser His Arg Trp Ala Leu Thr Ala
65 70 75 80

Bandman et al. SEQ ID: 3

-continued

```
                140                 145                 150

Asn Met Lys Pro Leu Gln Leu Tyr Arg Lys Gly Val Ile Lys Ala
                155                 160                 165

Thr Pro Thr Thr Cys Asp Pro Gln Leu Val Asp His Ser Val Leu
                170                 175                 180

Leu Val Gly Phe Gly Ser Val Lys Ser Glu Glu Gly Ile Trp Ala
                185                 190                 195

Glu Thr Val Ser Ser Gln Ser Gln Pro Gln Pro Pro His Pro Thr
                200                 205                 210

Pro Tyr Trp Ile Leu Lys Asn Ser Trp Gly Ala Gln Trp Gly Glu
                215                 220                 225

Lys Gly Tyr Phe Arg Leu His Arg Gly Ser Asn Thr Cys Gly Ile
                230                 235                 240

Thr Lys Phe Pro Leu Thr Ala Arg Val Gln Lys Pro Asp Met Lys
                245                 250                 255

Pro Arg Val Ser Cys Pro Pro
                260
```

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 314 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(vii) IMMEDIATE SOURCE:
(A) LIBRARY: PROSTUT03
(B) CLONE: 789927

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3 :

```
Met Gly Ala Arg Gly Ala Leu Leu Leu Ala Leu Leu Leu Ala Arg
                 5                  10                  15

Ala Gly Leu Arg Lys Pro Glu Ser Gln Glu Ala Ala Pro Leu Ser
                20                  25                  30

Gly Pro Cys Gly Arg Arg Val Ile Thr Ser Arg Ile Val Gly Gly
                35                  40                  45

Glu Asp Ala Glu Leu Gly Arg Trp Pro Trp Gln Gly Ser Leu Arg
                50                  55                  60

Leu Trp Asp Ser His Val Cys Gly Val Ser Leu Leu Ser His Arg
                65                  70                  75

Trp Ala Leu Thr Ala Ala His Cys Phe Glu Thr Tyr Ser Asp Leu
                80                  85                  90

Ser Asp Pro Ser Gly Trp Met Val Gln Phe Gly Gln Leu Thr Ser
                95                 100                 105

Met Pro Ser Phe Trp Ser Leu Gln Ala Tyr Tyr Thr Arg Tyr Phe
                110                115                 120

Val Ser Asn Ile Tyr Leu Ser Pro Arg Tyr Leu Gly Asn Ser Pro
                125                130                 135

Tyr Asp Ile Ala Leu Val Lys Leu Ser Ala Pro Val Thr Tyr Thr
                140                145                 150

Lys His Ile Gln Pro Ile Cys Leu Gln Ala Ser Thr Phe Glu Phe
                155                160                 165

Glu Asn Arg Thr Asp Cys Trp Val Thr Gly Trp Gly Tyr Ile Lys
                170                175                 180

Glu Asp Glu Ala Leu Pro Ser Pro His Thr Leu Gln Glu Val Gln
                185                190                 195
```

-continued

```
Val Ala Ile Ile Asn Asn Ser Met Cys Asn His Leu Phe Leu Lys
                200                 205                 210

Tyr Ser Phe Arg Lys Asp Ile Phe Gly Asp Met Val Cys Ala Gly
                215                 220                 225

Asn Ala Gln Gly Gly Lys Asp Ala Cys Phe Gly Asp Ser Gly Gly
                230                 235                 240

Pro Leu Ala Cys Asn Lys Asn Gly Leu Trp Tyr Gln Ile Gly Val
                245                 250                 255

Val Ser Trp Gly Val Gly Cys Gly Arg Pro Asn Arg Pro Gly Val
                260                 265                 270

Tyr Thr Asn Ile Ser His His Phe Glu Trp Ile Gln Lys Leu Met
                275                 280                 285

Ala Gln Ser Gly Met Ser Gln Pro Asp Pro Ser Trp Pro Leu Leu
                290                 295                 300

Phe Phe Pro Leu Leu Trp Ala Leu Pro Leu Leu Gly Pro Val
                305                 310
```

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 420 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(vii) IMMEDIATE SOURCE:
(A) LIBRARY: LUNGAST01
(B) CLONE: 877617

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4 :

```
Met Ser Pro Pro Pro Leu Leu Gln Pro Leu Leu Leu Leu Leu Pro
  5                  10                  15

Leu Leu Asn Val Glu Pro Ser Gly Ala Thr Leu Ile Arg Ile Pro
                20                  25                  30

Leu His Arg Val Gln Pro Gly Arg Arg Thr Leu Asn Leu Leu Arg
                35                  40                  45

Gly Trp Arg Glu Pro Ala Glu Leu Pro Lys Leu Gly Ala Pro Ser
                50                  55                  60

Pro Gly Asp Lys Pro Ile Phe Val Pro Leu Ser Asn Tyr Arg Asp
                65                  70                  75

Val Gln Tyr Phe Gly Glu Ile Gly Leu Gly Thr Pro Pro Gln Asn
                80                  85                  90

Phe Thr Val Ala Phe Asp Thr Gly Ser Ser Asn Leu Trp Val Pro
                95                 100                 105

Ser Arg Arg Cys His Phe Phe Ser Val Pro Cys Trp Leu His His
                110                 115                 120

Arg Phe Asp Pro Lys Ala Ser Ser Ser Phe Gln Ala Asn Gly Thr
                125                 130                 135

Lys Phe Ala Ile Gln Tyr Gly Thr Gly Arg Val Asp Gly Ile Leu
                140                 145                 150

Ser Glu Asp Lys Leu Thr Ile Gly Gly Ile Lys Gly Ala Ser Val
                155                 160                 165

Ile Phe Gly Glu Ala Leu Trp Glu Pro Ser Leu Val Phe Ala Phe
                170                 175                 180

Ala His Phe Asp Gly Ile Leu Gly Leu Gly Phe Pro Ile Leu Ser
                185                 190                 195
```